REMARKS/ARGUMENTS

Applicant's undersigned representative thanks Examiner Gibbs for the courtesy of the interview conducted with Applicant's representatives Donna Ward and Paul LeGaard on July 12, 2004.

After amendment, claims 1, 2, and 4-15 are pending. Claims 3 and 16-20 stand canceled. Claims 1 and 11 were amended to place the application in condition for allowance and to correct minor clerical errors. Support for these amendments is found in the original specification and specifically on page 11, lines 32-35. No new matter is added by these amendments.

Claim Objection

Claim 1 is objected to for the use of the term "lipprotein (a)"

Applicants respectfully request reconsideration and withdrawal of this objection for the following reason.

In an effort to place the application in condition for allowance, Applicants have amended claim 1 to correct a typographical error in three occurrences of the spelling of apolipoprotein.

Reconsideration of this objection is requested.

35 USC § 102(b) Rejection

Claims 1, 2, 11, 12, 14, and 15 are rejected under 35 USC § 102(b) over Morishita et al. (Circulation, 1998, 98:1898-1904).

The Examiner asserted that Morishita meets all of the structural requirements of the claims and is an inherent antisense compound.

Applicants respectfully request reconsideration and withdrawal of this rejection for the following reasons.

Applicants have amended claims 1 and 11 to recite antisense compounds that are 12 to 30 nucleobases in length and specifically hybridize with the nucleic acid molecule encoding human apolipoprotein (a). Claims 2, 12, and 14 depend either directly or indirectly from these claims and therefore include this embodiment.

Morishita is directed only to ribozymes (see, e.g., RZ120, RZ151, RZ164 and mRZ151) and to a DNA oligonucleotide (DNA-RZ151) that are each about 42 nucleobases in length. See, Morishita, page 1899, col. 1 under "Synthesis of Ribozyme ON and Selection of Sequence Targets". Morishita does not teach antisense compounds that are 12 to 30 nucleobases in length.

In fact, as Applicant's representative discussed with the examiner, even minimal ribozymes require about 40 nucleotides in length to properly operate (including the size of the stem-loop, catalytic region and antisense arms)[1]. Morishita therefore cannot and does not teach Applicants' invention.

Reconsideration of this rejection in view of the amendment is requested.

[1] See, e.g., T. Ohmichi and E. Kool, 2000 Nucl. Acids Res., 28 (3):776-783) (filed concurrently with Information Disclosure Statement).

35 USC § 103(a) Rejection

> Claims 1, 2, 4-10, and 12-15 are rejected under 35 USC § 103(a) over Morishita et al. (Circulation, 1998, 98:1898-1904) in view of Baracchini et al. (US Patent No. 5,801,154) and Fritz et al. (J. Colloid and Interface Science, 1997, 1965:272-288).

Applicants respectfully request reconsideration and withdrawal of this rejection for the following reasons.

A. Morishita teaches away from the present invention.

As stated above, Morishita's disclosure is limited to ribozyme oligonucleotides against Apo(a) that are about 42 nucleobases in length. Morishita describes its ribozyme technology as a ***novel*** therapeutic strategy.

Morishita does not teach or suggest antisense sequences to Apo (a) that are 12 to 30 nucleobases in length, because as discussed above, even minimal ribozymes require about 40 nucleotides in length to properly operate.

In fact, in emphasizing the benefits of its ribozyme strategy, Morishita states that "it ***appears to be*** very difficult to use antisense strategy" (page 1899, col. 1; emphasis added). Morishita provides no data to support its generic condemnation of antisense sequences which employ Apo(a) as a target.

Morishita is an ineffective reference for use in this obviousness rejection because not only do its compounds fail to meet all structural requirements of the amended claims, but Morishita teaches away from the antisense sequences of Applicants' amended claims.

B. The combination of Morishita and the Secondary References does not suggest the present invention.

Morishita in combination with the generic secondary references does not suggest the desirability of the invention of Applicants' amended claims, as required to make an obviousness rejection. See, MPEP §2143.01.

The two cited secondary documents teach nothing regarding human apolipoprotein (a) or antisense sequences capable of inhibiting human apolipoprotein (a) activity. Baracchini refers to antisense compounds that modulate another *completely unrelated protein* to human apolipoprotein (a), namely multidrug resistance-associated protein (MRP). Fritz refers to cationic nanoparticles as a carrier system for antisense compounds in general. Baracchini and Fritz do not teach or suggest anything about ribozymes or about antisense sequences targeted ***to Apo(a)*** that are 12 to 30 nucleobases in length.

This combination of Morishita's 42-mer ribozymes with the antisense sequences of Fritz and Baracchini does not suggest the 12 to 30 nucleobase antisense sequences of the amended claims of the present invention and the use thereof, nor present a reason for the desirability of the compounds of the present invention, or the use thereof.

The secondary references do not provide a motivation for one to modify the 42-mer anti-apo(a) ribozyme sequences of Morishita so that they meet the definition of antisense compounds of Applicants' claim 1. Nor does this combination of prior art provide any expectation that by doing so, one would obtain a successful outcome. Such modification of Morishita's ribozymes to force them to meet

the 12-30 nucleotide requirement of Applicant's amended claims would make the ribozymes ineffective for their intended purpose. See, e.g., footnote 1.

The combination of Morishita with the secondary references cannot be made in further view of the negative teachings of Morishita with regard to antisense sequences. Morishita's own words quoted above teach away from such an outcome. There is nothing in either Fritz or Baracchini to assist in overcoming this negative teaching about the use of antisense strategies applied to Apo(a).

Therefore, Applicants respectfully submit that this combination would **not** have motivated one of skill in the art to make or modify Morishita's compounds to meet the requirements of Applicants' amended claims. In fact, the person of skill in the art might draw the opposite conclusion. The motivation to make the sequences claimed by Applicants' is derived from Applicants' disclosure only. Applicants' disclosure cannot be used as the source for such motivation to make an obviousness rejection. Reconsideration and withdrawal of this rejection is requested.

In view of the above amendments and these remarks, Applicants' respectfully request that the examiner withdraw the outstanding rejections and permit the above pending claims to pass to issue in due course.

The Director is hereby authorized to charge any deficiency in any fees due with the filing of this paper or credit any overpayment in any fees to our Deposit Account Number 08-3040.

Respectfully submitted,

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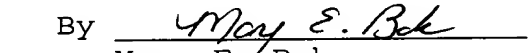
By 
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